REMARKS

The present invention is directed to pure ondansetron hydrochloride dihydrate. Claims 1-3 and 42-47 are pending in the application. New claims 48-50 are currently added.

Please note that a Notice of Appeal was filed July 23, 2004.

Following the suggested practice of MPEP § 706.07(h), this submission includes the amendments and arguments made in Applicants' Response to Final Office Action filed July 23, 2004. Further, this submission presents additional amendments to claims 1-3 and 42-47. Applicants respectfully request that the amendments as filed herewith be entered. If for any reason the amendments in Applicants' Response to Final Office Action were not entered, Applicants respectfully request that the unentered amendments not be entered.

As mentioned in Applicants' Response to Final Office Action filed July 23, 2004, Applicants file herewith a supporting declaration under 37 C.F.R. § 1.132.

Discussion of Final Office Action

In a Final Office Action dated January 23, 2004, the Office maintained the rejection of claims 1-3 and 42-47 under 35 U.S.C. § 103(a) as unpatentable over Chen (Zhongguo Yiyao Gongye Zazhi (1993), 24(6), pages 241-242), Tyers (U.S. Pat. No. 4,845,115) ("Tyers 1"), Coates (U.S. Pat. No. 4,695,578), and Tyers (U.S. Pat. No. 4,835,173) ("Tyers 2").

Amendments to the Claims

Applicants have cancelled claims 4-41 without prejudice. Applicants expressly reserve the right to pursue these claims in one or more divisional or continuation application(s).

Applicants have amended claims 1-3 and 42-47 limiting the claims to ondansetron hydrochloride dihydrate having an exo-methylene content of less than about 0.1%. The exo-methylene by-product is described in the specification at page 2, lines 15-16. Support for this amendment can be found at Example 4.

Applicants have rewritten claims 42-47 in independent form and added the solvent system to more particularly describe the present invention. Support for this amendment can be found, *inter alia*, at pages 8 and 10 of the specification and at originally filed claims 26, 27, 35, and 38.

Applicants have added new claims 48-50. These new claims are fully supported by the specification at pages 6-7, 9-10 and at originally filed claims 20 and 21.

Obviousness Rejection

Claims 1-3 and 42-47 have been rejected as obvious in view of Chen, Tyers 1, Coates, and Tyers 2. At page 4 of the Office Action, the Examiner states that "[t]he difference between the instant claimed invention and the prior art is that the prior art is silent as to the purity of the product obtained." The Examiner maintains the obviousness rejection "absent a showing of viable unexpected, unobvious and superior properties."

Ondanstetron hydrochloride dihydrate of high purity is a novel product that is not disclosed in the prior art. None of the references cited by the Examiner explicitly or implicitly disclose ondanstetron hydrochloride dihydrate with an exo-methylene content of less that about 0.1%. All of the references disclose the same inferior process that results in much greater quantities of the exo-methylene impurity. The inferior process (as exemplified by Coates) gives crude ondansetron hydrochloride dihydrate containing 0.4% exo-methylene. The Coates purification process gives ondansetron hydrochloride dihydrate containing 0.12% exo-methylene. In contrast, the purified ondansetron hydrochloride dihydrate of the present invention has only 0.01% or an undetectable amount of exo-methylene (see Example 4).

All of the prior art references cited by the Examiner use the solvent system of isopropanol and water. Applicants have discovered that by using the solvent system of water alone and by utilizing activated carbon, the purity and color of the product is significantly improved.

Also, all of the prior art references cited by the Examiner use about 3 equivalents of methyl-imidazole to prepare the ondansetron base starting material. Applicants have discovered that exo-methylene formation is inversely related to the amount of methyl-imidazole used to prepare the ondansetron base. By using about 4 to about 6 equivalents methyl-imidazole, Applicants obtained a product with significantly improved purity.

In view of the unexpected, unobvious, and superior purity of the claimed ondansetron hydrochloride dihydrate, Applicants respectfully request that the obviousness rejections be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present application is in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is invited to telephone the undersigned at the number below. The undersigned may also be contacted by email at dziker@kenyon.com.

Respectfully Submitted,

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